REMARKS

These remarks are in response to the Office Actions mailed June 5, 2002 and October 9, 2003. Claims 1 to 12 are pending. Claim 11 stands withdrawn as being directed to a non-elected invention. By the present amendment, claims 9, 11, 26 and 27 have been cancelled without prejudice. Applicants maintain the right to prosecute the canceled claims in any related application claiming the benefit of priority of the subject application. New claims 30 to 39 have been added. Accordingly, upon entry of the amendment, claims 1 to 8, 10, 12 to 25 and 28 to 39 are under consideration.

Applicants wish to thank the Examiner for the interview held on November 14, 2002, with the Examiner, the Examiner's supervisor and Applicants' representative. Applicants also wish to thank the Examiner for subsequent conversations between the Examiner and Applicants' representative. Applicants believe that the present amendment, including the amended and new claims, adequately address all issues discussed in the interview, and place the claims in condition for allowance.

Applicants remarks below are identical to the remarks made in the Response filed December 5, 2002. Applicants respectfully request reconsideration of the application.

Regarding the Claim Amendments

The amendments to the claims are supported throughout the specification or were made to address informalities. In particular, the amendment to claims 1 and 13 to recite "a blood coagulation protein" is supported, for example, at page 5, lines 23-26; and at page 9, lines 16-19, which discloses that proteins suitable for delivery include, for example, "any other blood coagulation protein." The amendments to claims 1 and 13 to recite that the immunosuppressive agent is administered "prior to or simultaneously" with said gene therapy "or before formation of said inhibitory antibodies" is supported, for example, at page 9, lines 20-22, which discloses that "the immunosuppressive agent is administered to the mammal prior to, and/or concomitantly with, and/or following administration of the gene therapy vector to the mammal;" at page 12, lines 11-13 which discloses that "the immunosuppressive agent is administered to the mammal for the purpose of preventing the formation of inhibitory antibodies to the delivered protein," therefore indicating that the immunosuppressive agent can be administered prior to the formation

of the inhibitory antibodies. The amendment to claim 1 to recite that the immunosuppressive agent comprises "cyclophosphamide or anti-CD40 ligand" was made to define the claim with greater particularity.

The amendment to claims 3 and 15 to recite that "an increase in Factor IX is observed" in the mammal is supported, for example, at page 8, lines 16-17, which discloses that "the vector is delivered to the mammal and the protein is expressed therein;" and at page 12, lines 10-11, which discloses that the administration of the gene therapy vector is for the "purpose of delivering a protein to a mammal," indicating that delivery of the vector increases protein expression in the mammal. The amendments conform claims 3 and 15 to the language suggested by the Examiner in the Office Action (see page 15, second paragraph). The amendments to claims 4 and 16, which depend from claim 1, were made to conform these claims to amended claim 1. Similarly, the amendment to claims 24 and 25 was made to conform these claims to amended claim 1.

Claim 10 has been amended in view of canceled claim 9 and, therefore the amendment addresses an informality. Claim 14 has been amended to no longer depend from claim 13. Claim 14, as amended parallels claim 13, except claim 14 recites "human." The amendment is therefore supported by claims 13 and 14. Claim 22 has been amended to depend from claim 13 instead of claim 21. The amendment addresses an informality as claim 21 recites a Markush group of immunosuppressive agents including cyclophosphamide.

Thus, as the claim amendments are supported by the specification or were made to address informalities, no new matter has been added. Furthermore, as the amendments were made to address all outstanding rejections, the amendments place the claims in better condition for allowance or appeal. Accordingly entry of the amendments is respectfully requested.

Regarding the New Claims

New claims 30 to 39 are presented for entry due to the amendment to claim 1. Claims 30 to 39, which ultimately depend from claim 14, are supported throughout the specification. In particular, claims 30 and 32 to 39 parallel claims 3 to 10 and 12, either prior to or upon entry of the present amendment, and, therefore, are supported by claims 3 to 10 and 12. Claim 31 is supported for the reasons set forth above for the amendment to claim 1. Thus, as new claims 30 to 39 are supported by the specification no new matter has been added. Entry of claims 30 to 39

is respectfully requested in light of the amendment to the claim 1 to place claim 1 and the claims depending therefrom in better condition for allowance or appeal.

Regarding the Drawings

The Examiner requests the filing of corrected Drawings. To comply with the Examiner's request, submitted herewith are corrected drawings prepared in accordance with PTO Form 948.

I. REJECTIONS UNDER 35 U.S.C. §112

The rejection of claims 1 to 13, 15, 24, 26 and 28 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement is respectfully traversed.

Claim 26 has been cancelled herein without prejudice. Accordingly, the rejection is moot in respect to claim 26. As to claims 1 to 13, 15, 24 and 28, the specification adequately enables these claims. Nevertheless, solely in order to further prosecution of the subject application, and without acquiescing to the propriety of the rejection, the claims have been amended as set forth above. The rejection will therefore be addressed insofar as they may pertain to the amended claims.

The Examiner indicates that these claims allegedly are only enabled for "multiple administrations" of the recited immunosuppressive agents (page 12, lines 1-2 of the Office Action). Applicants submit that the claims are enabled for single as well as multiple administrations of the recited immunosuppressive agents. In this regard, the specification exemplifies multiple administrations of the recited immunosuppressive agents. However, the reason for multiple administrations is to minimize potential toxic side effects to the animal, not because a single dose of the immunosuppressive agent is incapable of preventing formation of inhibitory antibodies. Thus, an increased single dosage of immunosuppressive agent can be administered to prevent formation of inhibitory antibodies. Accordingly, the skilled artisan would readily recognize that, by merely increasing the amount of the recited immunosuppressive agents, a single dose would prevent inhibitory antibody formation.

As to the grounds for rejection regarding the recitation of "a beneficial effect," Applicants respectfully point out the term "beneficial effect" refers to the result of Factor IX expression in the mammal. In this regard, a beneficial effect as set forth in the specification includes, for example, "a partial correction of aPTT," that is, a reduced clotting time (page 13,

lines 26-29). Thus, contrary to the Office Action (see page 9), that "one skilled in the art of gene therapy would interpret that the breadth of the term 'beneficial effect' to encompass[es] complete correction of a genetic defect," in view of the specification, one skilled in the art would recognize that complete correction of a genetic defect is not required. Accordingly, Applicants need not enable complete correction of a genetic defect. Nevertheless, amended claims 3 and 15 now recite that "an increase in Factor IX is observed," which the Examiner acknowledges is adequately enabled (page 4, lines 3-4 and page 9, lines 14-16 of the Office Action). Accordingly, in view of the amendment, these grounds for rejection are rendered moot.

In regard to Exhibit A (Herzog *et al.*, Molecular Therapy 4:192 (2001)), previously submitted with Applicants' Response filed March 8, 2002, being "not known at the time the invention was made," (page 14, last paragraph, of the Office Action), this exhibit was submitted to merely corroborate that the specification adequately enabled the claims. As pointed out in Applicants previous Response, the data in Exhibit A demonstrate that treatment of a dog with a combination of gene encoding Factor IX and cyclophosphamide blocked formation of anti-canine Factor IX antibodies resulting in sustained expression of Factor IX levels sufficient for partial correction of coagulation. Accordingly, that Exhibit A was published after the filing of the subject application is irrelevant since the exhibit merely corroborates the enabling disclosure of the specification.

In view of the aforementioned remarks and that the present amendment is believed to adequately address all outstanding grounds for rejection under 35 U.S.C. §112, first paragraph, Applicants respectfully request that the rejection be withdrawn.

The rejection of claims 1 and 13 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is respectfully traversed. The Examiner indicates that the term "said gene" lacks adequate antecedent basis.

Claims 1 and 13 have been amended to delete the recitation of "said gene." Accordingly, in view of the amendments, claims 1 and 13 are clear and definite. As such, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

II. REJECTION UNDER 35 U.S.C. §103(a)

The rejection of claims 13 to 23, 25, 27 and 29 under 35 U.S.C. §103(a) as allegedly unpatentable over High *et al.* (U.S. Patent No. 6,093,392) in further view of Smith *et al.* (Gene Therapy 3:496 (1996)) is respectfully traversed.

Claim 27 has been cancelled herein without prejudice. Accordingly, the rejection is moot in respect to claim 27. As to claims 13 to 23, 25 and 29, these claims would not have been obvious in view of High *et al.* alone, or in combination with Smith *et al.* For example, as pointed out in Applicants previous Response, High *et al.*, *inter alia*, do not describe that formation of inhibitory antibodies against a protein delivered via gene therapy can be prevented by administering an immunosuppressive agent.

Nevertheless, solely in order to further prosecution of the subject application, and without acquiescing to the propriety of the rejection, submitted herewith is a Statement to Establish Common Ownership of the subject application and U.S. Patent No. 6,093,392 executed by an authorized individual of the assignee of the subject application and U.S. Patent No. 6,093,392. The subject application was filed June 8, 2000. Thus, in accordance with 35 U.S.C. §103(c), as the subject application was filed after November 29, 1999, and the subject application and U.S. Patent No. 6,093,392 were commonly owned at the time of the invention, U.S. Patent No. 6,093,392 is not available as prior art against the subject application under 35 U.S.C. §102(e) or §103(a). Accordingly, as High *et al.* is not available as prior art and Smith *et al.* do not teach or suggest each and every element claimed, the rejection under 35 U.S.C. §103(a) must be withdrawn.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 1 to 8, 10, 12 to 25 and 28 to 39 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 509-4065.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-2212.

Respectfully submitted,

Date: 10-20-03

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